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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/642,763	08/19/2003	Francisco Veas	GRT/1721-67	3291

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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	PAPER NUMBER
1648	
MAIL DATE	DELIVERY MODE
11/06/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/642,763	VEAS, FRANCISCO	
	Examiner	Art Unit	
	LOUISE HUMPHREY	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-24,26-33,35-38 and 40-51* is/are pending in the application.

4a) Of the above claim(s) *45,46,48 and 49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-24,26-33,35-38,40-44,47,50 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the amendment filed 30 June 2008. Claims 1-21, 25, 34 and 39 have been cancelled. Claims 22-24, 26-33, 35-38 and 40-51 are pending. Claims 45, 46, 48 and 49 are drawn to a nonelected subject matter and hence are withdrawn from further consideration pursuant to 37 CFR 1.142(b). Claims 22-24, 26-33, 35-38, 40-44, 47, 50 and 51 are currently examined.

Claim Objections

The objection to the specification is **maintained** because Applicant only appended SEQ ID NO. to the sequence on page 13 but not to the sequences on page 17-19.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 22-24, 26-28, 41, 42 and 50 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement is **withdrawn** in consideration of the Applicants' argument.

The rejection of claims 41 and 51 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement is **withdrawn** in consideration of Applicants' argument.

The rejection of claims 22-24, 26-28, 42 and 50 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification commensurate in scope is **withdrawn** in consideration of Applicants' argument.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 22-24, 26-33, 35-37, 41, 42, 44, 50 and 51 under 35 U.S.C. §102(b) as being anticipated by La Casse *et al.* (15 January 1999) is **maintained** for reasons of record.

The instant claims are drawn to an immunogenic composition comprising a two-cell complex formed by interaction between a receptor-binding region and a receptor from a pathogenic agent, being expressed on the first and second cells, respectively, and further comprising an inert vehicle acceptable for administration to a mammal.

The instant claims are product-by-process claims and are not limited to the manipulations of the recited steps, only the structure implied by the steps. See MPEP § 2113:

> "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product

was made by a different process." In re Thorpe, 777 F.2d 695, 698,227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

La Casse *et al.* teach a co-culture of COS-7 cells transfected with plasmid vectors encoding HIV envelope protein gp120 and a second cell type transfected with plasmid vectors encoding the receptor U87-CD4-CCR5, which allows for cell-cell fusion. The cell complexes were fixed with 0.2% formaldehyde in phosphate-buffered saline (PBS) for immunization in mice. See page 361, 3rd column, Notes No. 9-12. PBS is an inert vehicle that can be administered to mammals. Sera were isolated from immunized mice. See page 359, 3rd column, line 7-19.

Response to Arguments

Applicant's arguments filed 30 June 2008 have been fully considered but they are not persuasive. Applicant argues that the Examiner was not aware of the retraction of LaCasse published results. However, Applicant has already presented this argument in the response filed on 10 September 2007. Therefore, this issue was addressed in the previous Office Action mailed on 28 December 2007 on page 13. Examiner's reasoning is being re-iterated as follows:

The retraction was about the neutralizing antibodies, which is not a claim limitation. Applicants are reminded that the claims are only directed toward an immunogenic composition comprising a two-cell complex formed by interaction between a receptor-binding region, being expressed on a first cell, and a receptor from a pathogenic agent, being expressed on a second cell. Applicants' arguments directed

toward the ability of the two-cell complex to induce neutralizing antibodies are not relevant because they are not claimed. In summary, Applicants argued that the cited prior art, La Casse *et al.* do not teach neutralizing antibodies. However, neutralizing antibodies is not germane to the patentability of the invention claimed in the instant application. Therefore, the prior art clearly teaches the claimed immunogenic composition comprising the two-cell complex. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993) (Claims to a superconducting magnet which generates a "uniform magnetic field" were not limited to the degree of magnetic field uniformity required for Nuclear Magnetic Resonance (NMR) imaging. Although the specification disclosed that the claimed magnet may be used in an NMR apparatus, the claims were not so limited.); *Constant v. Advanced Micro-Devices, Inc.*, 848 F.2d 1560, 1571-72, 7 "USPQ2d 1057, 1064-1065 (Fed. Cir.), cert. denied, 488 U.S. 892 (1988) (Various limitations on which appellant relied were not stated in the claims; the specification did not provide evidence indicating these limitations must be read into the claims to give meaning to the disputed terms.); *Ex parte McCullough*, 7 USPQ2d 1889, 1891 (Bd. Pat. App. & Inter. 1987) (Claimed electrode was rejected as obvious despite assertions that electrode functions differently than would be expected when used in nonaqueous battery since "although the demonstrated results may be germane to the patentability of a battery containing

appellant's electrode, they are not germane to the patentability of the invention claimed on appeal."). See MPEP §2145 (VI).

The rejection of claims 41 and 51 under 35 U.S.C. §102(b) as being anticipated by Thali *et al.* (1993) is **maintained**.

The instant claims are direct to an isolated serum or antibody formed against the composition obtained by interaction of a receptor-expressing cell and a target-expressing cell in contact with a binding agent. There are no claim limitations on the binding epitopes, so the instant claims read on any antibody including an anti-CD4-gp120 antibody, anti-CD4 antibody, anti-CCR5 antibody, anti-CXCR4 antibody, anti-gp120 antibody, anti-gp41 antibody, or anti-gp120/gp41 antibody.

Thali *et al.* teach antibodies 17b and 48d that targets a CD4-induced epitope on the gp120-CD4 complex but also binds isolated gp120. See page 3980. Thus, the instant invention is anticipated by Thali *et al.*

Response to Arguments

Applicant's arguments filed 30 June 2008 have been fully considered but they are not persuasive. Applicant argues that Thali's antibody was found in virally infected humans who do not appear to have been immunized with a cellular complex of target receptor and recognition region. However, it is unclear how this is related to or results in any difference between the claimed antibody and the prior art antibody. There are no claim limitations on the binding epitopes, so the instant claims read on any antibody

including an anti-CD4- gp120 antibody, anti-CD4 antibody, anti-CCR5 antibody, anti-CXCR4 antibody, anti- gp120 antibody, anti-gp41 antibody, or anti-gp120/gp41 antibody. Thali *et al.* clearly teach that antibodies 17b and 48d bind against a CD4-induced epitope on the gp120-CD4 complex and an isolated gp120, so these antibodies would bind a composition comprising a fusion intermediate formed between a first cell expressing gp120 and a second expressing CD4, just as claimed in claim 22. Applicant has not shown any structural difference between the claimed antibody and the prior art antibody.

Where, as here, the Patent Office lacks the facilities to perform comparisons between the claimed material and prior art materials that reasonably appear to meet the claim limitations, the burden is properly shifted to applicant to distinguish the claimed product from the prior art product. See *In re Best, Bolton, and Shaw*, 195 USPQ 430 (CCPA 1977); *Ex Parte Gray*, 10 USPQ2nd 1922 (BPAI 1989). Absent evidence to the contrary, it appears that the antibody of Thali *et al.* anticipates the instantly claimed invention. Patent owner's burden under the circumstances presented herein was described in *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977) as follows:

> Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. . . . Whether the rejection is based on 'inherency' under 35 U.S.C. §102, on 'prima facie obviousness' under 35 U.S.C. §103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products (footnote omitted).

The rejection of claims 41 and 51 under 35 U.S.C. §102(b) as being anticipated by Lee *et al.* (1997) is **maintained**.

Lee *et al.* teach a gp120-CD4-specific monoclonal antibody CG10. See page 6037, 2nd column, line 5-8. Thus, the instant invention is anticipated by Lee *et al.*

Response to Arguments

Applicant's arguments filed 30 June 2008 have been fully considered but they are not persuasive. Applicant argues that Lee's antibody is raised against a protein complex of soluble CD4-gp120 in contrast to the claimed antibody induced by a cellular complex. However, the instant claims do not limit the antibody to bind to any particular epitope on the two-cell-fusion complex, so the instant claims read on any antibody including an anti-CD4- gp120 antibody, anti-CD4 antibody, anti-CCR5 antibody, anti-CXCR4 antibody, anti- gp120 antibody, anti-gp41 antibody, or anti-gp120/gp41 antibody. Examiner agrees that Lee's antibody binds against a protein complex, which is the same as the immunogen in the claimed invention because the receptor/target on the claimed cells is also a protein complex. Applicant has not shown any structural difference between the claimed antibody and the prior art antibody. Absent evidence to the contrary, it appears that the antibody of Lee *et al.* anticipates the instantly claimed invention. Applicants need to provide some showing to distinguish the claimed invention from the cited prior art. Patent owner's burden under the circumstances presented herein was described in *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 22 and 40 under 35 U.S.C. §103(a) as being obvious over La Casse *et al.* (1999) in view of Rossio *et al.* (1994) is **maintained** for the same reason set forth above.

The instant claims are directed to an immunogenic composition comprising a two-cell-fusion complex fixed with aldidrithiol-2 (AT-2) after incubation.

The relevance of LaCasse *et al.* is set forth above. LaCasse *et al.* do not disclose the AT-2 fixing agent.

Rossio *et al.* describe the non-denaturing binding of HIV surface proteins using AT-2.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute AT-2 for formaldehyde for the advantage of this non-denaturing binding relative to denaturing binding agents such as formaldehyde as taught by Rossio *et al.* Therefore, the instant invention is obvious over LaCasse *et al.* in view of Rossio *et al.*

The rejection of claims 22-24, 26-33, 35-38, 40 and 41 under 35 U.S.C. §103(a) as being obvious over La Casse *et al.* (1999) in view of Riley *et al.* (1998) is **maintained** for the same reason as set forth above.

The instant claims are directed to an immunogenic composition comprising a two-cell-fusion complex formed between autologous mammalian first cells and HIV-infected second cells with a monoclonal antibody in replacement of a coreceptor.

The relevance of LaCasse *et al.* has been set forth above. Riley *et al.* disclose infecting human cells with HIV.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute human cells and HIV as the starting means for creating the antigen. The infection would exactly match the natural course of infection and would be expected to result in epitopes that mimic actual epitopes during natural infection. Further, if one were to raise antibodies in a mammal, one would expect that autologous cells as antigens would minimize the risk of microbial infection from a different donor as well as limiting the immune reaction to the new epitopes, rather than all of the antigens on the cells as would happen from a different donor. Therefore, the instant invention is obvious over LaCasse *et al.* in view of Riley *et al.*

The rejection of claims 24, 43, 44 and 47 under 35 U.S.C. §103(a) as being obvious over La Casse *et al.* (1999) in view of Murphy *et al.* (1990) is **maintained** for the same reason as indicated above.

The instant claims are directed to an immunogenic composition comprising a two-cell-fusion complex formed between second cells and first cells transformed baculovirus expressing CD4 and/or HIV coreceptors.

The relevance of LaCasse *et al.* has been set forth above. Murphy *et al.* disclose a baculovirus expression vector expressing HIV envelope genes and human CD4.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the composition of LaCasse *et al.* by expressing the HIV envelope genes and human CD4 in a baculovirus expression vector as taught by Murphy *et al.* The skilled artisan would have been motivated to do so to optimize the expression of the immunogens. There would have been a reasonable expectation of success, given that DNA constructs encoding CD4, gp120, gp160, and gp160 fragment cloned into the baculovirus expression vector pVL941 produced native HIV envelope proteins and recombinant human CD4 that interact with each other, as taught by Murphy *et al.* Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicant's arguments have been fully considered but are not persuasive. Applicant traversed all the rejections under 35 U.S.C. §103(a) using the same arguments against the primary reference, La Casse *et al.*, that the reference was not enabled because the results of neutralizing antibodies were retracted, which has been

addressed on pages 4-5 of this action. Therefore, each rejection is maintained for the same reason as set forth above.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/L. H./
Examiner, Art Unit 1648
27 October 2008
/Bruce Campell/
Supervisory Patent Examiner, Art Unit 1648